Patent Application Attorney Docket No. 34098/US/2 463077-00270 U.S. Express Mail No. EV 424739018 US

We Claim:

A composition comprising a prodrug agent comprising:

a) a protein that induces unwanted side effects due to undesired activity at or close to the site of administration:

b) a substantially non-immunogenic polymer;

c) a covalent labile linker between said protein and said polymer, wherein said polymer substantially interferes with the activity of said protein when said polymer is covalently linked to said protein.

said protein and said polymer are connected with one or more labile covalent bonds.

2. A composition according to claim 1 wherein said protein is capable of promoting the activation of antigen presenting cells.

3. A composition according to claim 2 wherein said protein is selected from the group consisting of endothelin, interleukin-1, interleukin-4, interleukin-8, interferon-gamma, macrophage-inflammatory protein, macrophage stimulating protien, matrix metalloprotienases, thrombopoietin, transforming growth factor-beta, tumor necrosis factor-alpha, and tumor necrosis factor-beta.

4. A composition according to claim 1 wherein said protein is capable of promoting the activation of T-cells.

5. A composition according to claim 4 wherein said protein is selected from the group consisting of interferon-gamma, interleukin-1, interleukin-2, interleukin-4, interleukin-6, interleukin-7, interleukin-9, interleukin-12, and interleukin-23.

6. A composition according to claim 1 wherein said protein is a growth factor capable of inducing cellular proliferation or differentiation.

7. A composition according to claim 6 wherein said protein selected from the group consisting of vascular endothelial growth factor, tumor growth factor-beta, insulin-like growth factor, fibroblast growth factor 2, 7, or 10, and bone morphogenic proteins 2, 4, 6, and 7.

8. A composition according to claim 1 wherein said substantially non-immunogenic polymer comprises polyethylene glycol.

9. A composition according to claim 1 further comprising a pharmaceutically acceptable carrier.

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- 10. A method for treating a disease comprising administration of a therapeutically effective amount of the composition of claim 9.
- 11. A method for treating a disease according to claim 10 wherein said administration is by subcutaneous injection, oral administration, or inhalation.